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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,217	09/15/2006	Ivan King	891-A-PCT-US	7034

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,217	KING ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/06,10/06,04/07, 05/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 1 and 15 are objected to because of the following informalities: In claim 1(a) the chemical name of the active agent should be recited followed by the notation in parentheses. This applies to the notation SCH66336 recited in claim 15 too. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a synergistic combination of VNP40101M with cytarabine (AraC) and fludarabine, does not reasonably provide enablement for a synergistic combination of VNP40101M with any other nucleoside. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art

(C) The level of predictability in the art
(D)The amount of direction provided by the inventor
(E) The existence of working examples
(F) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claims 17-18 are drawn to a synergistic combination of VNP40101M with an amount of a nucleoside. The term nucleoside is broad and is seen to include all nucleosides including structural analogs.

The state of the prior art

The examiner notes that prior art Gourdeau et al (US 6,630,480) and Hausheer et al (US 5,919,816) teach the use of nucleosides for the treatment of tumors and leukemias and that they can be combined with other antitumor agents. There is no teaching of potential synergistic combinations comprising nucleosides with other therapeutic agents.

The level of predictability in the art

There is not seen sufficient data to substantiate synergistic combinations between nucleosides and other antitumor agents. Based on the teachings of the prior art it is highly unpredictable as to which of the myriad of nucleosides when combined with another therapeutic agent will produce a synergistic composition.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable synergistic compositions as instantly claimed. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for predicting such combinations.

The specification (pages 2-4 and 7) mentions references for the instant active agent VNP40101M and other potential chemotherapeutic agents including nucleosides and their use for the treatment of tumors.

The existence of working examples

The working examples set forth in the instant specification are drawn to synergistic combinations of the instant active agent, VNP40101M with cytarabine and fludarabine (Tables 2 and 3 at pages 13-14 of the specification). Despite these examples there is little enabling disclosure for such a combination of the instant active agent with other nucleosides. Cytarabine and fludarabine and their combinations with the instant active agent are not representative of the entire class of nucleosides. Applicants are therefore not entitled to claim synergistic combinations of VPN40101M with all other nucleosides.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the synergistic compositions as instantly claimed. One of ordinary skill in the art would have to make all such compositions in order to determine which of the nucleosides and their amounts produce synergism with the instant active agent. Undue experimentation is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the term equivalent. In the absence of the specific structures or chemical names of the equivalents of this invention, the identity of said equivalents would be difficult to describe and the metes and bounds of the said equivalents applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in this and all other claims in which the said term is recited. The specification (pages 8-11) recites the said terms but does not provide a definition.

Claim 15 recites the names of therapeutic agents within parentheses. It is not clear if these are intended as limitations of the claim. If they are then the parentheses have to be deleted.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12 and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (International Journal of Toxicology, 2002, 21, 23-38; cited in the ISR of 10/19/2006) in view of Gourdeau et al (US 6,630,480) and Hausheer et al (US 5,919,816).

Lee et al teach that 1, 2-bis (methylsulfonyl)-1-(2-chloroethyl)-2-(methylaminocarbonyl) hydrazine (also abbreviated asVNP40101M) is a novel alkylating antitumor agent (abstract; page 23, right column, first paragraph). It has been shown to possess a broad spectrum of antitumor activity including solid tumors and leukemia (page 24, left column, middle paragraph). It has also been found to be superior to many other antitumor agents. Lee also teaches maximum tolerated doses of the agent. However, Lee et al do not suggest a combination of the compound with a nucleoside or a nucleoside analog and the use of the combination and another therapy for the treatment of tumors.

Gourdeau et al teach the use of cytosine analogs and cytarabine for the treatment of leukemia and chronic myelogenous leukemias (abstract; col. 5, line 10 through col. 7, line 56; col. 10, line 44 through col. 11, line 35). According to Gourdenau standard treatment for leukemia involves chemotherapy and/or radiation therapy and chemotherapy includes treatment with two or more anticancer drugs (col. 1, lines 55-63). Currently the most important nucleosides that are used for the treatment of leukemia are cytarabine, fludarabine, gemcitabine and cladribine (col. 2, lines 28-32).

Hausheer et al, drawn to antineoplastic agents, teaches several classes of antitumor agents including nucleosides, antimetabolites, camptothecin, etc. that are known to be used for treating tumors and cancers (col. 2, line 15 through col. 32, line 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make compositions of VNP40101M and a nucleoside or nucleoside analog and use the combination in methods of treatments as instantly claimed since compositions comprising the individual active agents and their use for the treatment of tumors, cancers and leukemias is seen to be taught in the prior art.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980.

It is well within the skill level of the artisan to adjust the dosage level of the active agents in order to obtain maximum beneficial effects.

Conclusion

Claims 1-12 and 14-21 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623